

Cascade diagrams for depicting complex interventions in randomised trials

Article (Published Version)

Hooper, Richard, Froud, Robert J, Bremner, Stephen A, Perera, Rafael and Eldridge, Sandra (2013) Cascade diagrams for depicting complex interventions in randomised trials. BMJ, 347. f6681. ISSN 1756-1833

This version is available from Sussex Research Online: <http://sro.sussex.ac.uk/id/eprint/54578/>

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the URL above for details on accessing the published version.

Copyright and reuse:

Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

RESEARCH METHODS & REPORTING

Cascade diagrams for depicting complex interventions in randomised trials

Clarity about how trial interventions are delivered is important for researchers and those who might want to use their results. A new graphical representation aims to help make complex interventions clearer

Richard Hooper *senior lecturer in medical statistics*¹, Robert J Froud *senior research fellow, clinical trials*^{2,3}, Stephen A Bremner *lecturer in medical statistics*¹, Rafael Perera *university lecturer in medical statistics*⁴, Sandra Eldridge *professor of biostatistics*¹

¹Centre for Primary Care and Public Health, Blizard Institute, Queen Mary University of London, London E1 2AT, UK; ²Clinical Trials Unit, Division of Health Sciences, University of Warwick, Warwick, UK; ³Norges Helsehøyskole, Campus Kristiania, Norway; ⁴Centre for Evidence Based Medicine, Department of Primary Health Care, University of Oxford, Oxford, UK

Many medical interventions—particularly non-pharmacological ones—are complex, consisting of multiple interacting components targeted at different organisational levels.^{1,2} Published descriptions of complex interventions often do not contain enough detail to enable their replication.²⁻⁵ Reports of behaviour change interventions should include descriptions of setting, mode, intensity, and duration, and characteristics of the participants.⁶ Graphical methods, such as that showing the relative timing of assessments and intervention components,⁷ may improve clarity of reporting. However, these approaches do not reveal the connections between the different “actors” in a complex intervention.⁸ Different audiences may want different things from a description of an intervention, but visualising relationships between actors can clarify crucial features such as the fidelity with which the intervention is passed down a chain of actors⁹ and possible routes of contamination between treatment arms. Here we describe a new graphical approach—the cascade diagram—that highlights these potential problems.

Hierarchical interventions

Figure 1a¹ is a schematic illustration of a hierarchically delivered intervention. At the top is a health professional or primary investigator who trains several health professionals at the next level down to deliver the intervention to a common standard. Each of these second level professionals then delivers the intervention to patients at the third level. In this example we suppose that patients are treated in groups: thus each patient receives input from a health professional (the arrow coming down from the second level) and also from the other patients

in their group (drawn as a circulating arrow at the lowest level), and these inputs combine or interact to produce a health benefit.

In fig 1b¹ we have uncluttered the diagram by separating out the information showing the relationships between actors at different levels. The circulating arrow allows us to show the contact between patients and the level at which it occurs without having to depict more than one patient. We can no longer see how many actors there are at different levels, or the range of their characteristics: these things are important to report, but current guidelines recommend that they be included in the CONSORT flowchart and in text or tables.^{6,10} What we are left with is a diagram showing the flow from the source of the intervention, at the top, down to the patient who receives it, at the bottom. This simple idea is the basis for the cascade diagram.

Figure 2a¹ shows the graphical elements that make up a cascade diagram: actors (rectangular boxes), hierarchical levels not represented by an actor (rounded boxes), and intervention components (arrows with labels, indexed in a separate key). As an example we illustrate in fig 2b a parenting intervention for preterm infants described by Johnson and colleagues.¹¹ In this study the trial manager trained research nurses in the delivery of the active intervention, and each nurse delivered the intervention to mothers of babies in neonatal intensive care units. Mothers then cared for their infants, whose cognitive outcomes were assessed at 2 years.

As a general rule, our diagrams exclude actors who provide only routine care, with no influence from any experimental intervention. In fig 2 we have excluded intensive care unit staff, who were not trained in the intervention. We have, however,

Correspondence to: R Hooper r.l.hooper@qmul.ac.uk

Example of cascade diagram and other types of graphical presentation for a real trial (see <http://www.bmj.com/content/347/bmj.f6681?tab=related#datasupp>)

included the neonatal intensive care units in the hierarchy because it allows us to show the extent of communication between mothers taking part in the study. The exchange of information between mothers is shown as a circulating arrow extending back as far (horizontally) as the level of the intensive care unit and no further, the assumption being that contact between mothers extends only as far as those attending the same unit, and not, for example, to those seen by the same research nurse.

The diagonal arrangement of actors denotes the cascade of an intervention through a hierarchy. Different actors at the same level, who do not stand in a hierarchical or sequential relationship to each other, can be shown one under the other, or side by side, depending on what works best in the diagram. We use singular rather than plural nouns in our actor boxes (“research nurse” rather than “research nurses”) to avoid ambiguity about who delivers the intervention. A box may contain more than one person if they interact jointly with the actor at the next level—for example, we might write “general practitioner and practice nurse” or simply “practice staff” if these were the people a patient had contact with—but we would recommend writing, for example, “midwife” rather than “midwives” unless each participant was seen by a whole team of midwives.

Trials

So far we have discussed how to illustrate the delivery of an active intervention, but we would like our diagrams to go further and show the different treatment arms in a trial. In fig 3 we illustrate our suggested approach using a variety of simple two arm trial designs.

Figure 3a shows the simplest kind of trial, with participants randomised individually. We indicate randomisation with a shaded banner running behind the two randomised groups. As before, we do not include actors who provide only routine care. In this example, the control participant is isolated graphically: there is no link through which he or she can receive the active intervention—that is, no possible route for contamination.

Figure 3b shows how an individually randomised design can lead to contamination in something like a general practice setting, where patients attending the same practice share information about the care they receive. Practice is shown as an organisational marker, with no actors at this level involved in delivering the intervention. Patient to patient contact within a practice is indicated by the circulating arrow, which shows information circulating within the bounds defined by a practice. Because there are control and intervention participants at the same practice, this circulating flow provides a route through which the active intervention can pass to, or contaminate, control participants.

Figure 3c shows how a cluster randomised trial avoids contamination in this situation.¹² If we assume that the flow of information between participants does not extend between clusters—in this case between patients at different general practices—then the circulating flow among control participants is effectively isolated from the flow among intervention participants. The diagram shows that there is no route through which the active intervention can pass to control participants.

Finally, fig 3d shows a cluster randomised trial in which the intervention is aimed at cluster (practice) level, its effects then being cascaded down to individual participants. Again, contamination is avoided by randomising in clusters.

More complex interventions

We developed cascade diagrams after considering how to describe real life trials of complex interventions. Here we illustrate one example, the Older People’s Exercise Intervention in Residential and Nursing Accommodation (OPERA) trial,¹³ which was a trial of an exercise programme to reduce depression. We consulted in depth on the graphical representation of OPERA with its chief investigators as well as those conducting a process evaluation of the trial, to produce summaries that they found helpful. The results are shown in the web appendix, where we present the cascade diagram, the diagram proposed by Perera and colleagues (the PaT plot),¹⁴ and the CONSORT flowchart for OPERA, to show how these approaches complement each other (the numbers in the CONSORT flowchart have been left blank, as these were unpublished at the time we developed the supplement).

The CONSORT flowchart, which should always be included in a trial report,¹⁰ summarises the flow of individuals through a trial, whereas the cascade diagram is a model of the flow of interventions. The PaT plot describes the timing of different intervention components, while the cascade diagram shows the relationships between the actors delivering them. Detailed information about intervention components is included in the key to the cascade diagram, which also acts as the key to the PaT plot. Between them, the cascade diagram, PaT plot, key, and CONSORT flowchart form a complete description of a trial of a multicomponent, multilevel intervention such as OPERA.

Even for a complex intervention, we suggest that the cascade diagram be kept as simple as possible. Actors who only provide routine care can be left out unless that care is contaminated by an experimental intervention, though we will always need to show, at the lowest level, the individual participant or unit of analysis. Different boxes referring to the same type of actor are needed when different actors are randomised into different arms; when the same actor fulfils more than one role in a trial, however, there should just be one box for that actor. The appearance of more than one of the same kind of actor in the diagram, unless at the randomisation level, alerts us to situations where actors are separated into non-randomised groups—for example, midwives at a maternity unit being divided non-randomly into those who treat intervention mothers and those who treat controls—a situation that should usually be avoided.

Discussion

We have introduced a simple but powerful graphical approach to describe the delivery of a complex intervention in a trial. The method focuses on aspects that are not well addressed by existing approaches to reporting.

A recent, evidence based assessment of the key dimensions in describing complex interventions distinguished between the timing of intervention components, for which a diagrammatic approach has already been successfully introduced,⁷ and other features—including “structure and architecture” and dependence on healthcare professionals—which our cascade diagrams attempt to depict.¹⁵ Cascade diagrams may be useful after a study as a tool facilitating implementation or evidence synthesis, and before a study to encourage researchers to reflect on their design.^{4–8} Managers considering how to adopt a published intervention can use the diagram to compare their institutional context with the one in which the intervention was evaluated.¹⁵ At the design stage researchers can show design choices and identify methodological problems such as contamination or

non-randomised groups—part of the crucial “modelling” phase in the development and evaluation of a complex intervention.¹⁶ Contamination arising through contact between individuals at one level of a hierarchy is not always a bad thing: at the level of individual participants it can help to reinforce an intervention; at an intermediate health professional level it can help to standardise it.

Cascade diagrams are particularly useful for describing interventions delivered in a hierarchical context and for those whose complexity arises from a truly complex system, not just a complicated one.¹⁷ For example, the diagram shows how, rather than flowing straight down a cascading sequence of actors, an intervention can be reinforced or altered by circulating currents within hierarchical levels. The box representing each actor in the diagram is a “black box”: arrows enter and leave but may combine inside the box in non-linear ways.

We have limited the range of graphical elements in the diagrams to make them as intuitive as possible, but researchers may want to play with them further—for example, different arrow styles could distinguish intervention components according to whether the standardisation being proposed was by function or form.^{15 18}

Graphical methods in general continue to interest researchers.^{18 19} Graphs and figures can be included as online extras in a journal article even when editorial policy limits the number of figures in the print version. Cascade diagrams have some features in common with Unified Modelling Language (UML) sequence diagrams, which are also beginning to find applications in health services research.²⁰ A Microsoft Word toolkit for producing cascade diagrams is available from the authors.

Commentators agree that much needs to be done to improve the reporting of trials of complex interventions.²⁻⁶ The more people are able to understand what other researchers have done, the more likely they are to reproduce, cite, and discuss this work. We offer our diagrammatic approach as one new tool to aid in this complex task.

We thank Martin Underwood and Stephanie Taylor, chief investigators of the OPERA trial, and David Ellard, who conducted a process evaluation of OPERA, for their input into the OPERA example. We also thank the reviewers of earlier manuscripts for helpful comments.

Contributors: RH conceived the graphical approach following a course on cluster randomised trials given by SE. The authors developed the method in consultation with clinical trialists, applying the method to real examples and revising it in the light of feedback from trialists, reviewers,

and others. RH led on writing the manuscript, and all authors contributed to the final version. RH is the guarantor.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and have no relevant interests to declare.

Provenance and peer review: Not commissioned; externally peer reviewed.

- Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. *BMJ* 2000;321:694-6.
- Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655.
- Pino C, Boutron I, Ravaud P. Inadequate description of educational interventions in ongoing randomized controlled trials. *Trials* 2012;13:63.
- Michie S, Fixsen D, Grimshaw JM, Eccles MP. Specifying and reporting complex behaviour change interventions: the need for a scientific method. *Implement Sci* 2009;4:40.
- Glasziou P, Meats E, Heneghan C, Shepperd S. What is missing from descriptions of treatment in trials and reviews? *BMJ* 2008;336:1472-4.
- Abraham C. WIDER recommendations. 2013. www.interventiondesign.co.uk/?page_id=9.
- Perera R, Heneghan C, Yudkin P. Graphical method for depicting randomised trials of complex interventions. *BMJ* 2007;334:127-9.
- Glasziou P, Chalmers I, Altman DG, Bastian H, Boutron I, Brice A, et al. Taking healthcare interventions from trial to practice. *BMJ* 2010;341:c3852.
- Bell AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, et al. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. *Health Psychol* 2004;23:443-51.
- Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Ann Intern Med* 2008;148:295-309.
- Johnson S, Whitelaw A, Glazebrook C, Israel C, Turner R, White IR, et al. Randomized trial of a parenting intervention for very preterm infants: outcome at 2 years. *J Pediatr* 2009;155:488-94.
- Donner A, Klar N. Cluster randomization trials. *Stat Method Med Res* 2000;9:2.
- Underwood M, Eldridge S, Lamb S, Potter R, Sheehan B, Slowther AM, et al. The OPERA trial: protocol for a randomised trial of an exercise intervention for older people in residential and nursing accommodation. *Trials* 2011;12:27.
- Perera R, Heneghan C, Yudkin P. PaT plot. 2013. www.cebm.net/index.aspx?o=4200.
- Wells M, Williams B, Treweek S, Coyle J, Taylor J. Intervention description is not enough: evidence from an in-depth multiple case study on the untold role and impact of context in randomised controlled trials of seven complex interventions. *Trials* 2012;13:95.
- UK Medical Research Council. Complex interventions guidance. 2008. www.mrc.ac.uk/complexinterventionsguidance.
- Shiell A, Hawe P, Gold L. Complex interventions or complex systems? Implications for health economic evaluation. *BMJ* 2008;336:1281-3.
- Hawe P, Shiell A, Riley T. Complex interventions: how “out of control” can a randomised controlled trial be? *BMJ* 2004;328:1561-3.
- Pitt M, Stahl-Timmins W, Anderson R, Stein K. Using information graphics in health technology assessment: toward a structured approach. *Int J Technol Assess Health Care* 2009;25:555-63.
- Kumarapeli P, de Lusignan S, Koczan P, Jones B, Sheeler I. The feasibility of using UML to compare the impact of different brands of computer system on the clinical consultation. *Inform Primary Care* 2007;15:245-5.

Accepted: 4 October 2013

Cite this as: *BMJ* 2013;347:f6681

© BMJ Publishing Group Ltd 2013

Figures

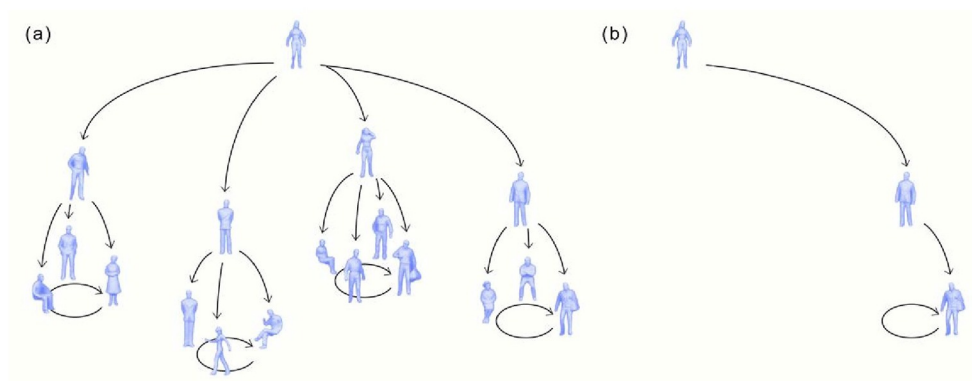


Fig 1 (a) Illustration of a hierarchically delivered intervention: a health professional or primary investigator at the top level trains several health professionals to deliver the intervention to a common standard; each second level professional then delivers the intervention to patients in a group setting. Circulating arrows show the intervention circulating within a group (the second level professionals are trained separately and independently, so there is no circulating arrow at this level). (b) Abstraction of the first diagram showing the relationships between actors at different levels

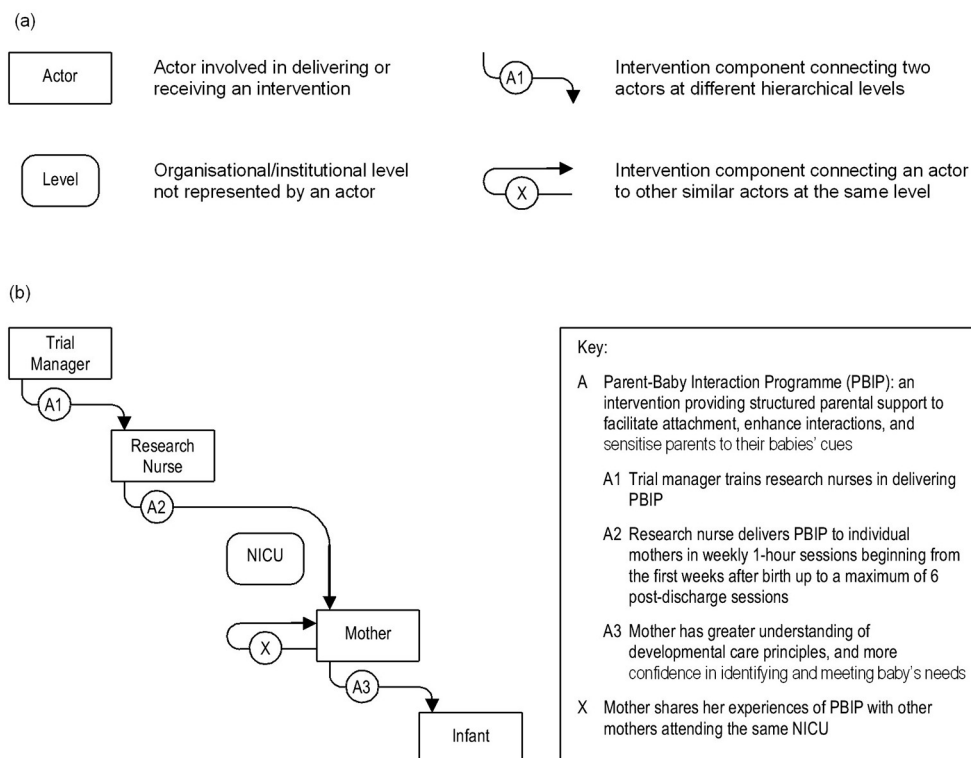


Fig 2 (a) Graphical elements making up the cascade diagram. (b) Cascade diagram for the parent-baby interaction programme (PBIP), a parenting intervention for very preterm infants in neonatal intensive care units (NICU)¹¹

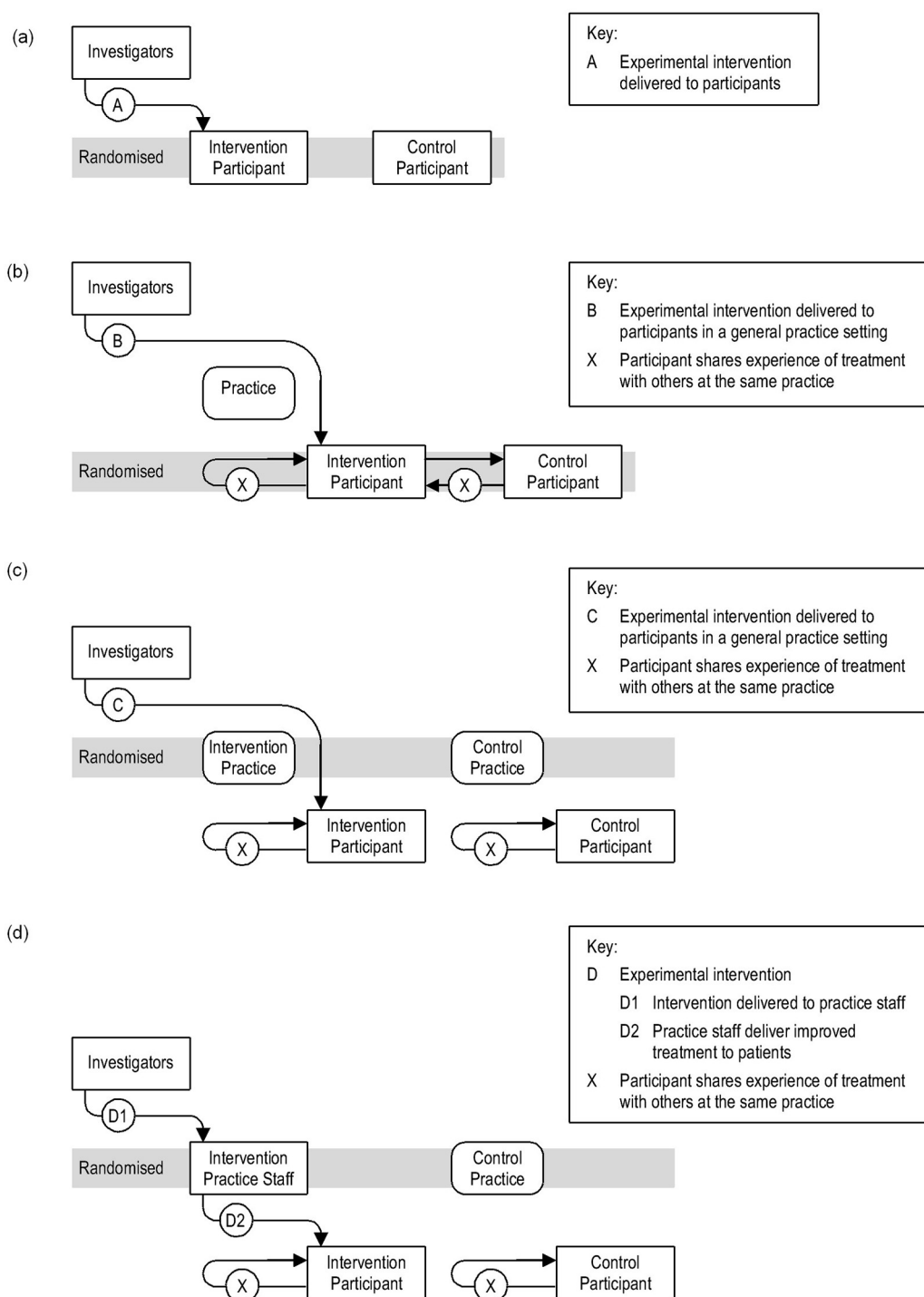


Fig 3 Cascade diagrams for various designs of randomised controlled trial: (a) a trial with individuals randomised to two arms; (b) an individually randomised trial in a general practice setting, showing contamination; (c) the same trial cluster randomised by practice; (d) a cluster randomised trial of an intervention delivered by general practice staff